Novel Approaches to Spectral Processing and Quantification

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Magnetic Resonance Spectroscopy (MRS) is increasingly being used as an adjunct to conventional imaging to provide information concerning the viability, proliferative status and functional behavior of living tissue for basic science, pre-clinical and clinical situations. Although the procedures for acquiring 1-H MRS data on animal and human scanners are fairly common, there are still no commercial standards for post-processing and quantitative analysis. This limits the ability to compare results across platforms and means that many studies are still either using qualitative analyses or taking their results offline for post-processing. A further complication for the interpretation of MRS data is the trend towards using multi-channel radiofrequency coils. While there are numerous possibilities for combining the contributions from different elements using parallel imaging reconstruction methods, there have been a relatively small number of applications to MRS data. This presentation will summarize the state of the art in reconstruction, analysis and interpretation of spectral data with an emphasis on novel approaches and future needs.

H-1 MR Spectroscopy of the Brain a 1.5T

The use of water suppressed H-1 spectroscopy has been facilitated by the availability of pulse sequences for PRESS and STEAM volume selection that can be used routinely in the brain in single or multi-voxel mode. While the data quality in regions that avoid the sinuses is generally good there are a number of artifacts that arise due to lipid contamination, motion and gradient imperfections. In a recent review, Kreis (1) provided an extensive description of the common spectral artifacts that can be observed with single voxel and multi-voxel spectral acquisitions in the brain. It is important that these artifacts become more widely understood so that the clinical interpretation of the data is accurate. Analysis of STEAM and PRESS datasets from the brain are typically performed using automated software packages (2-5). While model-based functions are typically such as LCModel and AMARES are typically used for fitting short echo time spectra (6-7), there are still challenges for short echo times in terms of managing the baseline components that arise due to the presence of macromolecules (8).

Although an increasing number of researchers are using echo planar or spiral k-space sampling approaches, these are not yet available for routine applications. These options are necessary for obtaining increased coverage and large 3-D matrix sizes within a relatively modest acquisition time but lead to challenges in terms of maintaining data quality and developing more sophisticated methods for quantification, reconstruction and post-processing. Ebel et al (9) showed that although automated processing of such data was possible and that a large region of the brain could be covered there were a relatively large percentage of voxels for which there was poor linewidth or significant lipid contamination. Other alternative k-space sampling strategies and methods for reducing lipid components and have been proposed recently, including changes in acquisition parameters and post-processing routines (10-14).

H-1 MRS at higher field strengths and from other organs

The increasing availability of clinical 3T MR scanners has provided spectra with higher signal to noise ratio from the brain (15-19). The T2 relaxation times of brain metabolites are longer at 3T than at 1.5T and so the actual increase in signal to noise ratio is less than a factor of two but there is typically improved spectral resolution (16), which leads to more reliable quantification of metabolites such as myo-inositol and glutamate using approaches such as J-resolved MRS with LCModel fitting (17-19).

While the brain is the most common region being studied with H-1 MRS, there are a substantial number of applications in the prostate at (20-22). Quantification of prostate spectra requires estimation of levels of choline, creatine and citrate. The parameter most commonly used to infer tumor versus normal or benign tissue is the ratio of (choline+creatine)/citrate. The majority of the studies to date have used frequency domain integration of peak regions as opposed to time domain fitting to obtain these values. A recent comparison of the two techniques showed that at 1.5T the accuracy of time domain fitting was improved for well shimmed spectra with high signal to noise ratio but that the simpler frequency domain approach was more robust, especially in the presence of the broad polyamine resonance in normal prostate tissue (23). The fitting of prostate spectral peaks is more challenging at 3T due to the strong coupling of the citrate resonances and requires either a change in acquisition parameters or more complex modeling of the spectral components (24-27).

There have also been an increasing number of applications of MRS to the breast at 1.5T and 4T (28-35). In this case the main resonance being observed is choline and the challenge is to suppress large lipid peaks and obtain at least a relative measure of peak intensity. Bolan et al have addressed this at 4T in a series of papers that have come up with a robust strategy for acquisition and quantification (31-34). Together with the work of Katz-Bull et al (29), these have laid the groundwork for more extensive clinical studies. Similar challenges are faced in other body applications. Preliminary studies in this regard have included liver, thorax, muscle, head and neck, and cervix (36-38).

Multi-channel H-1 MRS

The availability of MR scanners with multiple receive channels has expanded the usage of phased array coils and raised the question of how to best combined the signals from individual elements. As reviewed in the original papers (39-40), a variety of different approaches can be taken, depending on whether the goal is to provide phase sensitive spectra and to correct for spatial variations in intensity of the spectra due to the non-uniform rf profiles of individual coil elements (41-43). The latter requires estimates of the profiles of individual coils which can be obtained from theoretical estimates, empirical measurements in phantoms, by using residual water as a reference or by filtering of in vivo images that have been acquired with minimal (usually proton density weighted) contrast. For phase sensitive spectra it may be necessary to process each channel separately and then combine the results afterwards. This has been shown to be feasible but does require increased processing time.

The trend in MR imaging towards more rapid, multichannel acquisitions has provided a revolution in the use of so-called parallel reconstruction methods which make use of the fact that there is distinct spatial information in the individual coil elements. This can be used to reconstruct data with a higher resolution than would have been possible by simply taking the fourier transform of the original phase encoded arrays. This is particularly relevant at higher field strengths, where the increased signal to nose ratio means that larger acquisition matrices and/or faster scan times are feasible. Because MRSI uses phase encoding or other types of k-space sampling in multiple directions, it can benefit from speed-up factors in more than one dimension. Examples of the use of the SENSE were presented by Dydak et al (44-45). There are clearly trade-offs in terns of spectral artifacts and reconstruction times that must be considered in using such parallel approaches (46). These need to be studied further before these techniques are applied in a routine clinical setting.

Multinuclear MRS

The increased availability of MR scanners with in higher field strength has meant that there is beginning to be a resurgence of the applications of multi-nuclear MRS with a particular emphasis on P-31 (47) and C-13 (48-51) MRS. There have been relatively few new insights into the processing of such data beyond the use of fitting model functions with prior information, but this is likely to change as the number of studies being performed increases (52). A further motivation has been the promise of the availability of hyperpolarized C-13 tracers which is providing challenges in terms of having very high signal to noise ratio but requiring very rapid acquisitions (53). This field is just in its infancy but is of major interest for researchers engaged in developing data processing algorithms as it will need novel k-space sampling strategies, parallel reconstruction methods, time domain fitting of truncated signals and dynamic modeling of signal decay.

Tissue Classification by MRI and MRS

With the availability of a larger body of clinical MRS data there has been the need to apply multi-variate statistical techniques and artificial intelligence approaches to determining which metabolite peaks and which combination of imaging methods provide the most relevant information. The largest number of these has been to the analysis of data from brain tumors and has included consideration of the MRS data alone (54-59) or in conjunction with conventional MRI, perfusion MRI or diffusion MRI (60-65). The consensus is that high choline and low n-acetylaspartate distinguish tumor from normal tissue and that high lactate and lipid or low creatine are indicative of increased malignancy. This may be reflected in higher histological grade and/or worse outcome (61-65). Similar strategies are being applied to conventional MRI, dynamic contrast uptake imaging and MRS data from patients with prostate cancer and have shown that the MRS data definitely add to the diagnosis and ability to assess response to therapy (66-68). Methods such as canonical correlation analysis and neural networks are likely to play an increasing role in determining the clinical benefits of new MRI and MRS techniques (69-71).

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